

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference  2004.835 WO	<b>FOR FURTHER ACTION</b>		see Form PCT/ISA/220 as well as, where applicable, Item 5 below.
International application No.  PCT/EP2005/051766	International filing date (day/month/year)  21/04/2005	(Earliest) Priority Date (day/month/year)  23/04/2004	
Applicant  AKZO NOBEL N.V.			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

**4. With regard to the title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. With regard to the drawings,**

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2005/051766

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C07D209/40 C07D401/04 C07D403/04 C07D405/04 C07D413/04  
 C07D401/12 A61K31/40 A61P5/26 A61P15/16

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2004/041782 A (AKZO NOBEL N.V; HERMKENS, PEDRO, HAROLD, HAN; STOCK, HERMAN, THIJS; TE) 21 May 2004 (2004-05-21) cited in the application compounds 58, 99, 101-103, 105, 106 -----	1-33
A	WO 03/011302 A (MERCK & CO., INC; HUTCHINSON, JOHN, H; BRESLIN, MICHAEL, J; HALCZENKO,) 13 February 2003 (2003-02-13) claim 1 -----	1-33
A	WO 03/064387 A (F. HOFFMAN-LA ROCHE AG) 7 August 2003 (2003-08-07) claims 1,28 -----	1-33
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

5 August 2005

Date of mailing of the international search report

16/08/2005

Name and mailing address of the ISA  
 European Patent Office, P.B. 5818 Patentlaan 2  
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Authorized officer

Bakboord, J

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2005/051766

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHENGALVALA M ET AL: "Selective androgen receptor modulators" EXPERT OPINION ON THERAPEUTIC PATENTS, ASHLEY PUBLICATIONS, GB, vol. 13, no. 1, 2003, pages 59-66, XP002292692 ISSN: 1354-3776 cited in the application the whole document	1-33
P,A	EP 1 466 902 A (TAKEDA CHEMICAL INDUSTRIES LTD 'JP!') 13 October 2004 (2004-10-13) claim 1	1-33

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2005/051766

## Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 31-33  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 31-33 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/EP2005/051766

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004041782	A	21-05-2004	AU 2003301853 A1 WO 2004041782 A1	07-06-2004 21-05-2004
WO 03011302	A	13-02-2003	CA 2455179 A1 EP 1420796 A1 JP 2004538307 T WO 03011302 A1 US 2003065004 A1	13-02-2003 26-05-2004 24-12-2004 13-02-2003 03-04-2003
WO 03064387	A	07-08-2003	BR 0307406 A CA 2473803 A1 CN 1628113 A WO 03064387 A2 EP 1501826 A2 US 2003220319 A1	28-12-2004 07-08-2003 15-06-2005 07-08-2003 02-02-2005 27-11-2003
EP 1466902	A	13-10-2004	AU 2002367424 A1 CA 2471754 A1 EP 1466902 A1 US 2005101657 A1 WO 03057669 A1 JP 2003252854 A	24-07-2003 17-07-2003 13-10-2004 12-05-2005 17-07-2003 10-09-2003

PCT

To:

see form PCT/ISA/220

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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2005/051766

International filing date (day/month/year)  
21.04.2005

Priority date (day/month/year)  
23.04.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D209/40, C07D401/04, C07D403/04, C07D405/04, C07D413/04, C07D401/12, A61K31/40, A61P5/26,

Applicant  
AKZO NOBEL N.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 31-33

because:

☒ the said international application, or the said claims Nos. 31-33 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details



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**Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-33
	No: Claims	
Inventive step (IS)	Yes: Claims	1-33
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-30
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 31-33 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

V.1 The present invention relates to 3-thio-6-amino indoles useful in the treatment of androgen-receptor related diseases.

V.2 Reference is made to the following documents:

D1: WO 2004/041782 A (AKZO NOBEL N.V; HERMKENS, PEDRO, HAROLD, HAN; STOCK, HERMAN, THIJS; TE) 21 May 2004 (2004-05-21)

Document D1 was published after the priority date. In the presumption the priority is valid this document is not regarded as prior art.

D2: WO 03/011302 A

D3: WO 03/064387 A

D4: CHENGALVALA M: 'Selective androgen receptor modulators', Expert Opinion, vol. 13, no.1, 2003, pages 59-66, XP 002292692

D5: EP-A-1 466 902 (TAKEDA CHEMICAL INDUSTRIES LTD [JP]) 13 October 2004 (2004-10-13)

Document D5 was published after the priority date. In the presumption the priority is valid this document is not regarded as prior art.

**V.3 Novelty**

It is noted that document D1 discloses compounds of formula I (compounds 58, 99, 101-103, 105, 106) useful in the treatment of androgen-receptor related diseases. Document D2 discloses 4-aza steroid compounds as androgen receptor modulators.

Document D3 discloses substituted indoles of which the generic formula falls under the scope of the compounds of the present application but no examples are given falling under the scope of the present application. The compounds are alpha-1-agonists.

Document D4 discloses non-steroidal androgens.

It is noted that document D5 discloses pyrrole derivatives as androgen receptor antagonists.

A compound of formula I is disclosed in none of the documents. Claims 1-21 therefore fulfill the requirements of Art 33(2) PCT.

Claim 22 describes a compound of formula I for use in therapy and is novel by consequence.

Claims 23-26 describe a pharmaceutical composition comprising a compound of formula I and are novel by consequence.

Claims 27-30 describe the use of a compound of formula I for the manufacture of a medicament and are novel by consequence.

Claims 31-33 describe a method of treatment comprising administering a compound of formula I and are novel by consequence.

#### **V.4 Inventive step**

Starting from documents D2 and D4 the problem to be solved by the present application may be regarded as how to provide novel possibly improved androgen receptor modulators. The solution of the applicant resides in providing compounds of formula I. The applicant shows in table 1 that some compounds of the present application have androgenic activity. As the compounds of the present invention have not been made obvious by the prior art the solution of the applicant may be regarded as involving an inventive step (Art 33(3) PCT).

#### **V.5 Industrial applicability**

For the assessment of the present claims 31-33 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**VI Certain documents cited**

WO 2004/041782 A  
EP-A-1 466 902